

## **BRIMOPRESS**

**BRIMOPRESS** (Brimonidine Tartrate ophthalmic solution) 0.2% is a relatively selective alpha-2 adrenergic agonist for ophthalmic use.

### **CLINICAL PHARMACOLOGY**

#### **Mechanism of action:**

**BRIMOPRESS** is an alpha-adrenergic receptor agonist. It has a peak ocular hypotensive effect occurring at two hours post-dosing. Fluorophotometric studies in animals and humans suggest that Brimonidine Tartrate has a dual mechanism of action by reducing aqueous humor production and increasing uveoscleral outflow.

#### **Pharmacokinetics:**

After ocular administration of a 0.2% solution, plasma concentrations peaked within 1 to 4 hours and declined with a systemic half-life of approximately 3 hours. In humans, systemic metabolism of Brimonidine is extensive. Primarily the liver metabolizes it. Urinary excretion is the major route of elimination of the drug and its metabolites. Approximately 87% of an orally administered radioactive dose was eliminated within 120 hours, with 74% found in the urine.

### **INDICATIONS AND USAGE**

**BRIMOPRESS** is indicated for lowering intraocular pressure in patients with: -

1. Open-angle glaucoma
2. Ocular hypertension.

### **CONTRAINDICATIONS**

**BRIMOPRESS** is contraindicated in patients with hypersensitivity to Brimonidine Tartrate or any component of this medication. It is also contraindicated in patients receiving monoamine oxidase (MAO) inhibitor therapy

### **PRECAUTIONS**

#### **General:**

Although **BRIMOPRESS** had minimal effect on blood pressure of patients in clinical studies, caution should be exercised in treating patients with severe cardiovascular disease.

**BRIMOPRESS** has not been studied in patients with hepatic or renal impairment; caution should be used in treating such patients.

**BRIMOPRESS** should be used with caution in patients with depression, cerebral or coronary insufficiency, Raynaud's phenomenon, orthostatic hypotension or thromboangiitis obliterans.

#### **Drug Interactions:**

Although specific drug interaction studies have not been conducted with **BRIMOPRESS**, the possibility of an additive or potentiating effect with CNS depressants (alcohol, barbiturates, opiates, sedatives, or anesthetics) should be considered. Alpha-agonists, as a class, may reduce pulse and blood pressure. Caution in using concomitant drugs such as beta-blockers (ophthalmic & systemic), antihypertensives and/or cardiac glycosides is advised.

Tricyclic antidepressants have been reported to blunt the hypotensive effect of systemic clonidine. It is not known whether the concurrent use of these agents with **BRIMOPRESS** in humans can lead to resulting interference with the IOP lowering effect. No data on the level of circulating catecholamines after **BRIMOPRESS** instillation are available. Caution, however, is advised in patients taking tricyclic antidepressants, which can affect the metabolism and uptake of circulating amines.

#### **Carcinogenesis, Mutagenesis, impairment of fertility:**

Brimonidine Tartrate was not mutagenic or cytogenic in a series of in vitro and in vivo studies including the Ames test, chromosomal aberration assay in Chinese Hamster Ovary (CHO) cells, a host-mediated assay and cytogenic studies in mice, and dominant lethal assay.

#### **Pregnancy: Teratogenic Effects:**

Reproductive studies performed in rats with oral doses of 0.66 mg base/kg revealed no evidence of harm to the fetus due to **BRIMOPRESS**. Dosing at this level produced 100 times the plasma drug concentration level seen in humans following multiple ophthalmic doses.

There are no adequate and well-controlled studies in pregnant women. In animal studies, Brimonidine crossed the placenta and entered into the fetal circulation to a limited extent.

**BRIMOPRESS** should be used during pregnancy only if the potential benefit to the mother justifies the potential risk to the fetus.

**Nursing Mothers:**

It is not known whether Brimonidine is excreted in human milk; but in animal studies it was excreted in breast milk. **BRIMOPRESS** should be used during lactation only if the potential benefit to the mother.

**Pediatric Use:**

The safety and effectiveness of **BRIMOPRESS** have not been studied in pediatric patients below the age of 2 years. **BRIMOPRESS** is not recommended for use in pediatric patients under the age of 2 years.

**Geriatric Use:**

No overall differences in safety or effectiveness have been observed between elderly and other adult patients.

**ADVERSE REACTIONS**

Adverse events occurring in approximately 10-30% of the subjects, in descending order of incidence, included oral dryness, ocular hyperemia, burning and stinging, headache, blurring, foreign body sensation, fatigue/drowsiness, conjunctival follicles, ocular allergic reactions, and ocular pruritus. Events occurring in approximately 3-9% of the subjects, in descending order included corneal staining/erosion, photophobia, eyelid erythema, ocular ache/pain, ocular dryness, tearing, upper respiratory symptoms, eyelid edema, conjunctival edema, dizziness, blepharitis, ocular irritation, gastrointestinal symptoms, asthenia, conjunctival blanching, abnormal vision and muscular pain.

The following adverse reactions were reported in less than 3% of the patients: lid crusting, conjunctival hemorrhage, abnormal taste, insomnia, conjunctival discharge, depression, hypertension, anxiety, palpitations/arrhythmias, nasal dryness and syncope.

**OVERDOSAGE**

No information is available on overdosage in humans. Treatment of an oral overdose includes supportive and symptomatic therapy; a patent airway should be maintained.

**DOSAGE AND ADMINISTRATION**

The recommended dose is one drop of **BRIMOPRESS** in the affected eye(s) two times daily, if the IOP peaks in the afternoon, one additional drop can be instilled in the afternoon.

**HOW SUPPLIED**

**BRIMOPRESS** is supplied sterile in 5 ml lupolen transparent plastic bottles.

**NOTE:** Store in a cool, dry and dark place only.